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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,506	01/12/2001	Charlotte Kensil	8449-153	2171

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EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/760,506	KENSIL, CHARLOTTE	
	Examiner	Art Unit	
	Celine X Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31,33-38,40 and 44-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31,33-38,40 and 44-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 April 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/20/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 31, 33-38, 40 and 44-46 are pending in the application.

This Office Action is in response to the Amendment filed on 10/20/04.

Response to Amendment

The rejection of claims 31, 33-38, 40, 44-46 under 35 U.S.C 112 1st paragraph is maintained (but changed to the scope of enablement) for reasons discussed in the Office Action mailed on 4/20/04 and further discussed below.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31, 33-38, 40, 44-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting tumor growth comprising administering to an individual an effective amount of a composition comprising *Quillaja saponaria* saponin to the vicinity of the tumor, wherein said composition stimulates innate immunity, and wherein said composition does not contain a vaccine antigen, does not reasonably provide enablement for a method of treating cancer comprising administering to an individual in need thereof an effective amount of a composition comprising a *Quillaja saponaria* saponins, wherein said composition stimulates innate immunity, and said composition does not contain a vaccine antigen. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In response to this rejection, Applicant argues that *Quillaja saponaria* saponins are effective in treating cancer because the Kensil Declaration, filed December 30, 2003, provides *in vivo* data that supports the efficacy of the use of *Quillaja saponaria* saponins. Applicant argues that the examiner's position of the xenograft model is not predictive for the compound's usefulness in human is false because *In re Brana* concludes that "do not question the usefulness of any compound as an antitumor agent or provide any other evidence to cause one of skill in the art to question the asserted utility of applicant's compounds." Applicant asserts that similar to the situation in *In re Brana*, the Gura reference cited by the examiner merely discusses the therapeutic predictive value of *in vivo* murine tests, which does not cause reasonable doubt as to the asserted utility. Moreover, Applicant argues that the court states that "proof of an alleged pharmaceutical property for a compound by statistically significant tests with standard experimental animals is sufficient to establish utility" in response to PTO's position of the predictive value of animal models in *In re Brana*, thus, since the Kensil Declaration provides experimental results demonstrating that QS-21 has antitumor activity in two different standard tumor models, it is sufficient to establish utility for the compounds. Applicant asserts that the P815 and Meth A tumor model used in the Kensil Declaration is a valid tumor model in pre-clinical drug development according to the citation of Kimura et al., Mescher et al., Nakagawa et al., Rakmilevich et al., and Gjewski et al. Furthermore, Applicant argues that Lynch and Leon cited by the examiner does not correlate with the ability of a single agent to treat cancer. Applicant asserts that *Quillaja saponaria* saponins can be used to treat a variety of cancers

because the Kensil Declaration demonstrates the utility of QS-21 to treat cancer in a fibrosarcoma and mastocytoma mouse model. In response to the examiner's rejection over the use of chemically modified *Quillaja saponaria* saponins, Applicant argues that the second Kensil Declaration submitted herewith provides evidence that *Quillaja saponaria* saponins share a common structure that gives rise to the common innate immunity function, and thus would be expected to function in the same manner with respect to increasing innate immunity and treating cancer. Applicant further asserts that the teaching of prior art provides guidance in terms of what kinds of modifications can be made to *Quillaja saponaria* saponins without adversely affect their immune adjuvant activity, and modification such as the ones taught by Soltysik would be predicted to be effective in treating cancer. Applicant thus concludes based on the teaching of prior art, the experiments presents in the Declarations, one skill in the art would know how to use the claimed invention according to the teaching of the specification.

These arguments have been fully considered and deemed partially persuasive. The claimed method is enabled to the scope given above. While the Kensil Declaration provides the *in vivo* data demonstrating administering Q21 intratumorally or in the vicinity of the tumor site inhibited tumor growth in the mouse, it does not enable the claimed invention to its full scope because it fails to demonstrate that the cancer is "treated." The claims are drawn to a method of "treating cancer...an individual in need thereof," which encompasses both preventing and treating cancer. In other words, since any individual who does not want to have cancer is "in need thereof" for such administration, prevention of tumor development is also encompassed by the claimed method. However, the data provided by Kensil Declaration and the instant specification does not provide sufficient enablement for such method of treating cancer. The

tumor size stays the same upon intratumorally injection of Q21 (see Figure 1 and 2). Injection of Q21 to the vicinity of the tumor site prior and following to tumor inoculation and postponed tumor development compared to the PBS control. Such data suggest Q21 is able to inhibiting tumor growth when administered in the vicinity of the tumor; therefore, the claimed invention is enabled for this scope.

In response to Applicant's argument in reference to *In re Brana,* the examiner acknowledges that the predictive value of the mouse model used in the Kensil Declaration does not affect the utility of the *Quillaja saponaria* saponins for their tumor inhibiting activity. However, Applicant is reminded that the instant claims are drawn to method of treating cancer rather than the chemical compounds claimed in *In re Brana.* As such, the standard for the enablement is a little different from that of the claimed compounds because the instant specification needs to provide enablement for the prevention and treatment of cancer *in vivo.* The specification only discloses that Q21 and Q7 stimulate NK cell activity, whereas the Declaration provides support for a method of inhibiting tumor growth. None of which demonstrate the enablement of a method of treating cancer. As such, the claimed invention is enabled to the scope as indicated.

The examiner acknowledges that *Quillaja saponaria* saponins share common structure that gives rise to the common innate immunity function according to the teaching of the second Kensil Declaration and cited references. However, the examiner does not agree that such common structure would be expected to function in the same manner with respect to increasing innate immunity and treating cancer. The second Kensil reference and the cited references demonstrate the common structure shared by the *Quillaja saponaria* saponins with regard to

their ability of enhancement of adaptive immunity in the context of using them as adjuvant, not as cancer treating compound. The chemical modification of the Q21 taught by Soltysik is also related to its immuno-potentiating activity as an adjuvant. The data presented in the 1st Kensil declaration demonstrate for the first time to use Q21 as an tumor inhibiting agent by itself. In view of the unpredictability in the field of cancer treatment discussed previously, whether any chemically modified form of *Quillaja saponaria* saponin has cancer treatment activity is unpredictable. Therefore, the claimed invention is limited to the scope indicated above.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

DAVE TRONG NGUYEN
PRIMARY EXAMINER

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.
Examiner
Art Unit 1636

DAVE TRONG NGUYEN
PRIMARY EXAMINER